

**TO  
THE CHAIRPERSON OF THE SCIENTIFIC JURY  
ANNOUNCED BY ORDER No. 15-05-93/26.09.2023  
TO THE EXECUTIVE DIRECTOR AND THE PROCURATOR  
OF ACC UMHAT TOKUDA EAD**

**REVIEW**

**by Professor Dr. Georgi Todorov Popov, PhD  
Head of The "Infectious Diseases" clinic - UMHAT Sofiamed**

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**SUBJECT:** Procedure for acquiring the educational and scientific degree "Doctor", Higher Education Region 7. "Health and Sports", Professional Direction 7.1 "Medicine", scientific specialty "Internal Diseases" announced by order of the Executive Director and the Procurator of ACC UMHAT Tokuda EAD No. 15-05-93/26.09.2023

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Pursuant to Order No. 15-05-93/26.09.2023 of ACC UMHAT Tokuda EAD, in my capacity as a member of the scientific jury, I have been assigned to submit a review regarding the procedure for defending a dissertation thesis for the acquisition of an educational and scientific degree "PhD", in the scientific specialty "Internal diseases" of Dr. Parvoleta Krasteva Yakova-Krasteva. The review has been compiled in accordance with the requirements of LDASRB, RILDASRB and the Regulations for the terms and procedure for acquisition of scientific degrees and holding of academic positions in ACC UMTAH Tokuda EAD.

Regarding the procedure for acquiring the educational and scientific degree "PhD" of Dr. Parvoleta Krasteva Yakova-Krasteva, I declare that I have no conflict of interest within the meaning of Art. 4, para. 5 of the Law on the Development of the Academic Staff in the Republic of Bulgaria (LDASRB). I have no publications in common with Dr. Parvoleta Krasteva Yakova-Krasteva.

**1. Biographical data and qualification of the candidate**

Dr. Parvoleta Krasteva Yakova-Krasteva was born on 24.06.1972. She graduated in medicine with a master's degree in MU-Sofia in 1996 (Medical University-Sofia - Diploma reg. no. 01678/ 17.03.1997). She began her professional career as a doctor in the Center for Emergency Medical Assistance - Sofia. On 01.12.2006, she started working as a doctor in the Emergency Department of Tokuda Hospital, Sofia, and from 30.03.2017. is the Head of the Emergency Department at ACC UMHAT Tokuda EAD, Sofia. For the period 2000 - 2005, she specialized in Emergency Medicine at the Medical University - Sofia, and since 2005 she has been a specialist in Emergency Medicine with Diploma No. 009951/ 01.20.2005. Since 2019, she has been enrolled as a doctoral student in independent training in the professional field "Medicine", doctoral program "Internal Diseases" at ACC UMHAT Tokuda EAD. The topic of the dissertation thesis is "Place and role of an emergency department of a multidisciplinary

active treatment hospital in the application of a diagnostic-therapeutic algorithm in patients over 18 years of age infected with SARS-COV-2 virus during pandemic" In the course of her professional development, Dr. Krasteva has a number of certified postgraduate studies, directly related to the scientific specialty of Emergency Medicine and its practical application.

The various aspects of Dr. Krasteva's professional development, presented in her biography, are reflected in the discussions of the activities performed by the contestant in the present review.

## **2. General presentation of the procedure and the doctoral student**

The presented set of materials on paper and electronic media is in accordance with Art. 115 (1) of the Procedure for the acquisition of ESD "PhD" in ACC UMHAT Tokuda EAD; Regulations of ACC UMHAT Tokuda EAD and includes the following documents:

- Application to the director and procurator of ACC UMHAT Tokuda EAD for admission to an official public defense of a dissertation thesis;
- Curriculum vitae in European format with the doctoral student's signature;
- Notarized copy of higher education diploma;
- Order for enrollment in doctoral studies and for deduction with right of defense;
- Order for conducting an exam from the individual plan and corresponding protocol;
- Protocol for passing the doctoral minimum in the specialty;
- Order on the composition of the extended scientific collegium of a clinic under the WB and minutes of a meeting held for deduction with the right of defense;
- Dissertation thesis;
- Abstract;
- List of scientific publications on the topic of the dissertation;
- Copies of scientific publications on the topic of the dissertation (with the doctoral student's signature);
- List of participations in scientific forums.
- Certificate of received credits from the group study plan;
- Declaration of originality and authenticity of the attached documents (signed by the doctoral student);
- Declaration of originality and authenticity of the dissertation thesis (signed by the supervisor of the doctoral student);
- Official reference from plagiarism platform.

To participate in this competition, the candidate submits a list of a total of 8 titles, including a dissertation and an abstract, 4 scientific articles and 2 participations with reports and posters in international and national scientific events. The qualitative characteristics of the presented publications are of a high scientific and scientific-applied level.

I believe that there is a clear personal participation of the doctoral student in the conducted dissertation research, especially in the sections materials and methods and results of the conducted scientific survey. I am convinced that the formulated contributions and obtained results are her personal merit.

The abstract is well structured, all chapters of the dissertation are included in abbreviated but meaningful form and reflects the main results achieved in the dissertation.

## **3. Relevance of the topic**

After a newly emerged strain of a virus belonging to the family Coronaviridae, the cause of a previously unknown acute respiratory disease, was isolated in the Wuhan region of China in December 2019, science has intensified its interest in this infection. The new etiological agent is named SARS-CoV-2. On 11/02/2020, the WHO officially renamed the disease that causes this virus to COVID-19. On March 11, 2020, the WHO declared COVID-19 a pandemic that continues to this day and affects all countries around the world. Current data on the

epidemiology, clinical picture, diagnosis and treatment of COVID-19 are constantly being updated and enriched. The SARS-CoV-2 virus has become the most studied virus by researchers around the world.

The evolution of the virus so far shows that it will not disappear, it will continue to circulate among the human population, constantly mutating and changing. This results in the appearance of new variants and sub-variants, and the disease has gone through 6 epidemic waves so far.

The study is up-to-date, with scientific contributions regarding the triage of patients with COVID-19; algorithms for laboratory diagnosis of patients with COVID-19; algorithms for imaging studies of patients with COVID-19; the algorithms for women entering labor sick with COVID-19; the algorithms for ambulatory administration of monoclonal antibodies to patients with COVID-19; initial definitive algorithm in patients with COVID-19;

#### **4. Knowing the problem**

In a multidisciplinary hospital for active treatment during a pandemic, the emergency department is where patient flow is filtered and directed in order to preserve overall hospital operations, ensure a safe working environment for staff, and patient security and peace of mind. The primary role of emergency physicians in the overall diagnostic-therapeutic algorithm for COVID-19 is diagnostic testing, interpretation of laboratory and imaging studies in the context of the clinical picture to differentiate patients by disease severity, and approximate progression risk prediction in order to the correct decision for therapeutic behavior is made. The doctoral student demonstrates excellent knowledge of the state of the problem and evaluates creatively used literary material.

#### **5. Research methodology**

The chosen research methodology allows achieving the set goal and obtaining an adequate answer to the tasks solved in the dissertation work.

#### **6. Characterization and evaluation of the dissertation work and contributions**

In the modern world, SARS CoV-2 has become one of the leading causes of respiratory infections. In the current pandemic, we have gone through 6 epidemic upsurges for the disease caused by the virus - COVID-19, related to the great mutagenic potential of the virus and the induced emergence of new variants and sub-variants of SARS CoV-2. The clinical spectrum of the disease ranges from mild, self-limiting respiratory infections to severe, life-threatening conditions with a hyperinflammatory response and severe pulmonary failure and death. All this has led to increased interest, intensive studies in the field of etiology, pathogenesis, diagnosis and search for new therapeutic and preventive strategies.

I believe that the aim to study and identify the early prognostic factors affecting the morbidity and survival of patients infected with SARS-CoV-2, with a view to developing a sufficiently effective, easily accessible and rapid algorithm for the primary clinical assessment of patients in Emergency Department, as well as the tasks set are too ambitious and well argued and defended in the subsequent chapters of the dissertation work.

The doctoral student has included a sufficient number of 6280 patients with COVID-19, passed and treated in the Emergency Department of ASK UMBAL Tokuda EAD, with etiologically verified SARS-CoV-2, for a period of nearly 2 years (11/03/2020 - 30/11 /2021). The study period covered patients infected with the original SARS-CoV-2 variant and the

currently dominant Delta variant, responsible for a large number of cases and more deaths worldwide.

Particularly valuable in the dissertation thesis is the analysis and actual application of the triage process (differentiation of patients) in the Emergency Department of a large multidisciplinary hospital during a pandemic. The implementation of quality triage is the basis and irreplaceable tool of the efficient management of the patient flow, especially in epidemic conditions. On the other hand, a challenge is the simultaneous service of all urgent and emergency patients passing through the emergency department to ensure the normal functioning of the multidisciplinary hospital. In Bulgaria, there are no general protocols for the triage of patients, and there is no uniform form for triage in emergency departments. A significant achievement in the work of the Emergency Department is that in the COVID zone, retriage and determination of triage category is carried out, and patients with unstable hemodynamic indicators are directed immediately to the COVID-room with opportunities to start oxygen therapy and/or resuscitation actions, and the stable ones patients are placed in the examination waiting area and reassessed every 30 minutes by a nurse. Even more valuable in the developed emergency department triage algorithm is the ability to direct clinical thought to the possibility of modifying this algorithm and applying it whenever another specific infectious agent is suspected.

As a clinician actively working with COVID-19 patients, I note with satisfaction the studied 171 patients in the acute period of the disease, who were administered monoclonal antibodies (MAB) in outpatient settings. It is highly relevant to initiate early specific therapy in ED outpatients to reduce viral load and prevent complications from COVID-19. Since November 2021, monoclonal antibodies have been administered in the CO of "ACC UMHAT Tokuda" EAD - initially ReGn-CoV2 (Casirivimab/Imdevimab), and subsequently Regkirona (Regdanvimab). Monoclonal antibodies have been used to treat non-hospitalized patients with mild to moderate-severe COVID-19 who are at high risk of developing severe disease. They help terminate the progression of viral replication, preventing progression to the hyperinflammatory stage of COVID-19, causing severe disease in high-risk non-hospitalized patients. The data that in 87.13% of patients, the early application of MAB prevented the development of severe disease and the need for continued treatment in hospital settings, correlates with the data of other authors.

A very good impression is made by the fact that 69 of the patients referred for home-ambulatory treatment had a control examination and 37 (53.62%) of them were hospitalized after it. In the group of patients with a control examination, the factors leading to progression and subsequent hospitalization were analyzed with the prognostic factors for complicated course and progression of COVID-19 discussed in the literature. The demographic factors age and gender were analyzed, the influence of comorbid diseases on the course of the disease and on its outcome was tracked. Of the comorbidities, the impact of comorbidities with COVID-19 was studied: arterial hypertension, diabetes mellitus, obesity, presence of ischemic heart disease (CHD), cerebrovascular disease (CVD), peripheral arterial disease (PAD), acute renal failure/chronic renal failure (ARF/CRF)/hemodialysis, chronic obstructive pulmonary disease (COPD), cancer. In the study, the relationship between worsening of the clinical condition, the subsequent hospitalization after a control examination and the presence of arterial hypertension before the disease was proven. The higher heart rate of the patients at the initial examination in

CO was a factor of borderline significance. These data correlate with the data of other authors from Bulgaria and abroad.

The present scientific work is based on the analysis of categorical variables and quantitative parameters in patients, easily measurable in the Emergency Department for primary clinical risk assessment and making effective decisions about therapeutic behavior in the conditions of the COVID-pandemic, according to the available human resource and material hospital base . Based on the analyzed prognostic factors, algorithms have been developed to identify high-risk patients and make a decision on therapeutic behavior when it is impossible to hospitalize all infected patients. Algorithms are especially valuable: for emergency department triage; for laboratory diagnostics; for imaging; for behavior in pregnant women going in for delivery; for ambulatory administration of MAB; to discharge patients from the Emergency Department. Particularly valuable in the developed algorithms is the fact that they can be transformed for all respiratory diseases with epidemic potential and in general for all acute infectious diseases.

I consider particularly valuable the contributions of a scientific and applied nature, namely: the risk factors affecting morbidity and survival in patients with COVID-19 over 18 years of age in the Emergency Department were tracked and analyzed. Knowing and actively looking for potential clinical predictors of increased mortality at the first meeting with the patient leads to a better therapeutic effect.

I place a high value on the credibility of the material on which the contributions of the dissertation work are based.

## CONCLUSION

The dissertation contains scientific, scientific-applied and applied results, which represent an original contribution to science and meet **all the requirements** of the Law on the Development of the Academic Staff in the Republic of Bulgaria (LDASRB), the Regulations for the Implementation of LDASRB and the Regulations of ACC UMHAT Tokuda EAD. The presented materials and dissertation results fully correspond to the specific requirements adopted in connection with the Regulations of ACC UMHAT Tokuda EAD for the application of LDASRB.

The dissertation thesis shows that the doctoral student Dr. Parvoleta Krasteva Yakova-Krasteva possesses in-depth theoretical knowledge and professional skills in the scientific specialty "Internal Diseases", demonstrating qualities and skills for independent conduct of scientific research.

Due to the above, I confidently give my **positive assessment** of the conducted research, presented by the above-reviewed dissertation work, abstract, achieved results and contributions, and I propose to the Honorable Scientific Jury to award the educational and scientific degree "PhD" to Dr. Parvoleta Krasteva Yakova- Krasteva in a doctoral program in "Internal Diseases".

Sofia

Prepared the review:

01/11/2023

Prof. Dr.  Popov, PhD